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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,131	09/26/2006	Audrey Royere	0512-1347	7355

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YOUNG & THOMPSON
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EXAMINER	
CRAIGO, WILLIAM A	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
07/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,131	ROYERE ET AL.	
	Examiner	Art Unit	
	WILLIAM CRAIGO	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-33,35-38 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-33,35-38 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *30 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 21, 27-30, 32-33, and 35-37 and 40 have been amended and are pending. Claim 39 was cancelled.

Withdrawn Rejections

Rejections not expressly maintained in this action are withdrawn.

New Rejections Necessitated by Amendment

Applicant's amendment of claim 37 to further limit the method of claim 21 necessitates new grounds of rejection. Applicant's amendment of claim 40 to depend from claim 21 necessitates new grounds of rejection. Applicant's amendment of instant claim 22 necessitates new grounds of rejection for claims 22-24. Applicant's amendment of instant claim 32 and 33 necessitates new grounds of rejection.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 40 is rejected under 35 U.S.C. 102(b) as being anticipated by Collins, WO 03/106809.

The rejection of claim 21 under 102(b) cited in the previous office action and from which instant claim 40 has been amended to depend is maintained, see response below.

Collins, pg. 6, lines 18-27, discloses the inclusion of ethanol in the emulsion which may be extractable into the primary oil phase, meeting the limitation of an organic phase which comprises a pharmaceutically active ingredient wherein the pharmaceutically active ingredient is selected from sedative and diuretic (instant claim 40).

Claims 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins WO 03/106809 A1.

Collins, pg. 6, lines 18-27, discloses the inclusion of ethanol in the emulsion which may be extractable into the primary oil phase, ethanol meets the limitation of pharmaceutically active ingredient and as it is not capable of forming particles at standard temperatures and pressures, it is reasonable to conclude the microspheres produced in Collins inherently meet the limitation of "are constituted in majority by the biodegradable polymer". Collins, example 2 discloses microparticles comprising polylactide-co-glycolide (compare instant claims 23-24).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Collins, WO 03/106809 A1 in view of Bibette, US 5938581.

Collins is directed to the preparation of chemicals encapsulated in a continuous polymeric phase (i.e. a microsphere) comprising a degradable polymer.

Example 2 and claim 1 of Collins describes the steps of preparing an emulsion comprising an organic phase with an active ingredient (a water soluble or water dispersible oil, water dispersible means that there is an organic phase separate from the aqueous phase), and a degradable polymer (example 2 teaches polylactide-co-glycolide, a biodegradable polymer) and an aqueous phase. Collins does not teach the recited viscosity; however, since the composition of the emulsion taught in Collins appears to be the same and prepared in the same manner as recited in instant claim

21, it is reasonable to conclude that the composition taught in Collins inherently posses' the viscosity ratio claimed because compound inherent properties are immutable. Thus the burden is shifted to applicant to provide objective evidence to show that the emulsion as taught by Collins does not inherently posses the viscosity ratio claimed. See MPEP 2112, V.

Example 2 teaches high shear mixing (i.e. controlled laminar shearing), then dispersing the emulsion in an aqueous phase/allowed to stir overnight (meeting the limitation of removing the organic solvent), and isolating the microparticles (i.e. microspheres, Collins, claim 5).

Collins, pg. 6, lines 18-27, teaches the inclusion of ethanol in the emulsion which may be extractable into the primary oil phase, meeting the limitation of an organic phase which comprises a pharmaceutically active ingredient (instant claim 21) and the limitations of sedative and diuretic (instant claim 40).

Collins does not expressly teach the use of a Couette device for the controlled shearing; however, Couette devices were known in the art for the preparation of emulsions.

Bibette is directed to emulsion manufacturing processes (title).

Bibette, example 9, teaches the use of a Couette cell to prepare a primary emulsion. Bibette, col. 6, lines 1-6 teaches a Couette cell allows continuous preparation of a secondary emulsion; thus the skilled artisan could have selected a Couette device for industrial production of the emulsion.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the prior art elements of Collins and Bibette according to known methods to yield the predictable result of providing a method for preparing monodisperse microspheres as instantly claimed because Collins teaches methods and materials directed to preparing emulsions and Bibette teaches a device which allows industrial production of emulsions.

Accordingly, the subject matter of instant claim 37 would have been prima facie obvious to one of ordinary skill at the time the invention was made, particularly in the absence of evidence to the contrary.

Claims 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins, WO 03/106809 A1 in view of Lobo, US 5589322 and Okada, US 5643607 as applied to instant claims 29 and 30 (see maintained rejections).

Okada, Example 1, teaches a method of providing microcapsules comprising 7.5 mL dichloromethane (density = 1.326 g/mL) = 9.945 g of dichloromethane; 4 g polylactide (polymer) and 400 mg TAP-144 (pharmaceutically active ingredient). Okada teaches the organic phase is about (4g polymer/4g polymer + 9.945g dichloromethane x 100% =) 28.7 % by weight of the polymer (compare instant claim 32). Similarly, Okada teaches gives guidance to provide a pharmaceutically active ingredient which is about (400 mg active ingredient/ 4g polymer+9.945g dichloromethane x 100% =) 2.87 % relative to the weight of the organic phase. While Okada does not expressly teach the active ingredient is part of the organic phase, the skilled artisan would have been aware of the fact that the distribution of the

pharmaceutically active ingredient will be dictated by the physical properties of the compound selected.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the wt% ratios as taught in Okada to provide the predictable result of providing a method for producing monodisperse microspheres as instantly claimed because Collins, Lobo, and Okada are all directed to methods and materials for providing emulsions and Okada provides express guidance to provide an emulsion comprising an active ingredient as instantly claimed.

Accordingly, the subject matter of instant claims 32-33 would have been prima facie obvious to one of ordinary skill at the time the invention was made, particularly in the absence of evidence to the contrary.

Maintained Rejections

Response to Arguments

Applicant argues Colins does not disclose the emulsions comprise a pharmaceutically active ingredient, this is not persuasive because Collins, pg. 6, lines 18-27, discloses the inclusion of ethanol in the emulsion which may be extractable into the primary oil phase, meeting the limitation of an organic phase which comprises a pharmaceutically active ingredient (instant claim 21).

Applicant argues Collins does not disclose a single emulsion, this is not persuasive because a single emulsion is disclosed in Collins (example 2) which is subsequently used to prepare the secondary emulsion. As instant claim 21 is open to

other steps (i.e. preparing a double emulsion from the single emulsion), Collins meets the limitations of amended claim 21.

The rejection of claims 21, 25-28, 31, 34-36 and 38 under 35 U.S.C. 102(b) as being anticipated by Collins, WO 03/106809 A1, 24 December, 2003 is maintained.

Applicant argues Collins and Lobo do not describe microspheres comprising a pharmaceutically active compound; this is not persuasive because Collins discloses the inclusion of ethanol in the emulsion and Lobo suggests the use of the emulsion method for use in medicine (col. 3 line 61).

Applicant argues the microspheres of Okada and Collins are prepared from a double emulsion; this is not persuasive because Okada and Collins teach single emulsions are made to produce the double emulsion and the method of instant claim 21 does not exclude other steps from the claimed method.

Applicant argues Lobo and Okada do not suggest monodisperse microspheres; this is not persuasive because Lobo teaches viscosities meeting the limitation of instant claim 21 and teaches monodisperse particles: see lines 54-57 “The emulsion can be then subjected to wall membrane formation to produce microcapsules with a desired particle size and a narrow particle size distribution.” Lobo teaches the method produces “monodisperse” microparticles (particles with a narrow size distribution).

Text of Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 21, 25-28, 31, 34-36 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins, WO 03/106809 A1, 24 December, 2003.

Collins is directed to the preparation of chemicals encapsulated in a continuous polymeric phase (i.e. a microsphere) comprising a degradable polymer.

Example 2 and claim 1 of Collins describes the steps of preparing an emulsion comprising an organic phase with an active ingredient (a water soluble or water dispersible oil, water dispersible means that there is an organic phase separate from the aqueous phase), and a degradable polymer (example 2 teaches polylactide-co-glycolide, a biodegradable polymer) and an aqueous phase. Collins does not teach the recited viscosity; however, since the composition of the emulsion taught in Collins appears to be the same and prepared in the same manner as recited in instant claim 21, it is reasonable to conclude that the composition taught in Collins inherently posses' the viscosity ratio claimed because compound inherent properties are immutable. Thus the burden is shifted to applicant to provide objective evidence to show that the emulsion as taught by Collins does not inherently posses the viscosity ratio claimed. See MPEP 2112, V.

Example 2 teaches high shear mixing, then dispersing the emulsion in an aqueous phase/allowed to stir overnight (meeting the limitation of removing the organic solvent), and isolating the microparticles (i.e. microspheres, Collins, claim 5).

Collins, pg. 6, lines 18-27, teaches the inclusion of ethanol in the emulsion which may be extractable into the primary oil phase, meeting the limitation of an organic phase which comprises a pharmaceutically active ingredient (instant claim 21)

Collins meets the limitations of of instant claim 21.

Collins, example 2 teaches the biodegradable polymer with a molecular weight of 65,000 daltons meeting the limitations of the range recited in claim 25.

Collins, claim 9, teaches ethyl acetate meeting the limitations of instant claim 26.

Collins, claim 1, teaches a water-dispersible oil as an active ingredient therefore meeting the limitation of lipid soluble, meeting the limitations of instant claim 27.

Collins, claim 1 teaches a water-soluble oil as an active ingredient meeting the limitations of instant claim 28.

Collins, example 2, pg. 31 teaches a double emulsion wherein the organic phase represents roughly 30% (15g (10ml dichloromethane)/ 50g (50ml aqueous phase)) meeting the limitations of instant claims 31 and 34.

Collins, example 2 teaches an external aqueous phase with a stabilizing agent (polyvinyl alcohol) meeting the limitations of instant claims 35 and 36.

Collins, example 2, teaches the dilution of the primary emulsion by 50ml of an aqueous solution of polyvinyl alcohol and Tween 80, effectively extracting the organic solvent into the aqueous phase. The microparticles are then washed with 300ml aliquots of water during recovery of the microparticles. The reference teaches removing the solvent from the organic phase by extraction in water meeting the limitations of instant claim 38.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 25-28, 31, 34-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins, WO 03/106809 A1, 24 December, 2003 in view of Lobo, US 5589322 A, 31 December, 1996.

Collins does not explicitly teach the emulsion has a ratio of organic to aqueous phase viscosity in the range of 0.1 to 10; however, Lobo teaches (examples 1-3) viscosity ratios, q, listed in the tables, between 0.1 and 10. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the known technique of modifying the viscosity ratio of organic to aqueous phases as taught in Lobo to improve the emulsion method of Collins to produce monodisperse microspheres because Lobo teaches the viscosity ratio is correlated to the particle size produced, i.e. by adjusting the viscosity ratio, one can adjust the size of the microspheres produced. Thus Collins teaches a method of producing a monodisperse population of microspheres and Lobo teaches a method of controlling the size of the microspheres produced. By modifying the method of Collins with the viscosity ratio as taught in Lobo one of ordinary skill is able to provide a monodisperse population of microspheres of a predictable size. Accordingly, the claimed invention of claims 21, 25-28, 31, 34-36 and 38 was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Claims 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins, WO 03/106809 A1, 24 December, 2003 in view of Lobo, US 5589322 A, 31 December, 1996 as applied to claims 21, 25-28, 31, 34-36 and 38 above, and further in view of Okada, US 5643607, 1 July, 2997.

Neither Collins nor Lobo disclose an active ingredient which is a peptide or protein (instant claim 29), nor a hydrophilic active ingredient in combination with a lipophilic active ingredient (instant claim 30).

Okada teaches the delivery of polypetides from microcapsules (i.e. microspheres) prepared by a water in oil emulsion (abstract). The physiologically active peptides disclosed by Okada, col. 2, line 17-67 include proteins (two or more amino acid residues and a molecular weight of about 200 to 100,000, insulin etc.). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the physiologically active peptides as taught in Okada for the active ingredients taught in Collins with the modified viscosities as taught by Lobo to obtain the predictable result of providing monodisperse microspheres as in instant claim 29 because all of the documents are directed to solving the problem of providing microparticles by emulsion technology. Further a protein is comprised of hydrophilic active ingredients in combination with lipophilic active ingredients because proteins are made up of amino acids some of which are hydrophilic, for example arginine, and some are lipophilic, for example phenylalanine. Since amino acids are active ingredients in and of themselves and proteins are combined amino acids the proteins taught in Okada meet the limitation of a hydrophilic active ingredient in combination with a lipophilic active ingredient as recited in instant claim 30. Accordingly, the claimed invention of claims 29 and 30 was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to WILLIAM CRAIGO whose telephone number is (571)270-1347. The examiner can normally be reached on Monday - Friday, 7:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

/WILLIAM CRAIGO/
Examiner, Art Unit 1615